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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/974,798 | 10/12/2001 | Ellen M. Heath | GSIM-01P-0014 | 7769 |

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VIKSNINS HARRIS & PADYS PLLP
P.O. BOX 111098
ST. PAUL, MN 55111-1098

| EXAMINER | |
|---|---|
| KHARE, DEVESH | |
| ART UNIT | PAPER NUMBER |
| 1623 | |

DATE MAILED: 09/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/974,798 | HEATH ET AL. | |
| | Examiner | Art Unit | |
| | Devesh Khare | 1623 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-45* is/are pending in the application.

4a) Of the above claim(s) *1-20 and 44* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-38,42,43 and 45* is/are rejected.

7)☒ Claim(s) *39-41* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/27/05;09/07/04.*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

This application has filing date as 10/12/2001.

The applicant's petition dated 05/18/2004 for withdrawal of Notice of Abandonment based on failure to receive an Office action mailed on 09/09/2003 has been granted.

***Response to Election with Traverse***

Applicant's election with traverse of the method for purifying RNA from biological material using an RNA lysing solution defined by Group II (claims 21-43 and 45) dated 06/16/2003 is acknowledged. The traversal is on the ground(s) that "the search and examination of the claims of Groups I and II can be made without serious burden". This is not found persuasive because the applicants claims encompass two distinct classes of methods for purifying RNA : (1) a method for purifying RNA from biological material with an RNA binding solution, classified in class 536; and (2) a method for purifying RNA from biological material with an RNA lysing solution, classified in classes 435 and 536, this method having an extra step of lysing the cells and release the nucleic acids including RNA, which would be burdensome to the examiner as it cannot be assumed that the modes of purification for one method of purification would be the same for another method of purification. The requirement is still deemed proper and is therefore made FINAL.

Claims 1-20 and 44 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

An action on the merits of claims 21-43 and 45 is contained herein below.

***Obviousness-type Double Patenting Rejection***

1. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

*Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).*

**Claims 21-25,27-30 and 45** are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 189 of co-pending U.S. Application Ser. No. 09/154,830 ('830).

Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims in each of the instant application (claims 21-25,27-30 and 45) and the '830 co-pending application (claims 1 and 189) are directed to substantially the same subject matter, i.e., in the instant claims, the invention is claimed in terms of a method for purifying undegraded RNA from biological material comprising the steps of:

mixing the biological material with an RNA lysing solution, forming a lysate, contacting lysate to an immobilized non-silica solid support; or contacting a biological material containing RNA with a solid support pre-treated with an RNA lysing solution, washing

the solid support with an RNA wash solution and eluting the bound RNA from solid support, while in the '830 co-pending application it is claimed in terms of a process for obtaining purified nucleic acids comprising the steps of:

contacting a sample containing nucleic acid with a solid support pre-treated with an lysing solution, loading the solid support into a sample processing container, purifying the nucleic acid, isolating the nucleic acid from solid support and collecting the nucleic acid. The specification of '830 discloses the source of the sample containing nucleic acid claimed in claims 22-25 on page 4 (line 2) and page 7 (lines 5-8). The non-silica solid support of instant claims 27-29 is also disclosed on page 5 (lines 1-5) in the specification of '830. The vessel or container containing the solid support of claim 30 is disclosed on page 7 (lines 9-11) in the specification of '830. Regarding the RNA Lysing Solution of instant claims 21 and 45, the specification of '830 discloses the use of the Lysing solution from Gentra Systems, Inc (page 5, lines 6-7). The nucleic acid lysing solution from Gentra Systems, Inc. is well known to be free of hazardous material such as strong chaotropic substance therefore the instant RNA Lysing solution of claims 21 and 45 (assignee Gentra Systems, Inc.) is inherently effective in order to form a lysate containing RNA from a biological material and free of any strong chaotropic substance. It would have been obvious to one having ordinary skill in this art, at the time the claimed invention was made to have optimized the amounts of the buffer and said RNA lysing solution to produce RNA from a biological material in combination with a solid support to accomplish a purified nucleic acid such as RNA of the '830 co-pending application which have the same use and effect. One of ordinary skill in the art would be

motivated to accomplish said method of purification since the beneficial effects of the active agents is individually taught in the prior art.

The examiner notes the instant claims and said claims of the co-pending U.S. Application '830, of applicants do indeed substantially overlap therefore this obviousness-type double patenting rejection is necessary to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees.

Therefore the claims are co-extensive.
This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

***35 U.S.C. 112, second paragraph rejection***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> *The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.*

Claims 21-38,42,43 and 45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.
(1) The term "substantially" in claims 21, 32 and 45 is relative, and the recitation of same renders the claim indefinite. The terms "substantially" is not defined by the claim,

the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention with regard to the substantially pure or pure and undegraded RNA.

(2) Regarding claims 21 and 45, the phrase "preferentially" renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. Dependent claims drawn to preferred limitations would be more favorably considered. See MPEP § 2173.05(d).

(3) Claim 31 recite the limitation "the strong chaotropic substance" of claim 21. There is insufficient antecedent basis for this limitation in the claim. There is no mention of the use of a strong chaotropic substance in the method of claim 21. Either the step wherein the method comprises the use of a strong chaotropic substance should be recited in Claim 21 or Claim 31 should be cancelled.

(4) Claims 42 and 43 recite the limitation "the RNA binding solution" of claim 21. There is insufficient antecedent basis for this limitation in the claim. There is no mention of the RNA binding solution in claim 21. Either the step wherein the purification comprises a binding solution should be recited in Claim 21 or Claims 42 and 43 should be cancelled. Therefore, the claims 42 and 43 are not been further treated on the merits.

(5) Regarding claims 21(c) and 45 (a), the phrase "such that" renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d). The phrase also renders claims depending from claim 21 indefinite.

Claims which depend from an indefinite claim which fail to obviate the indefiniteness of the claim from which they depend are also seen to be indefinite and are also rejected for the reasons set forth supra.

Claims 39-41 are objected to since they are dependent on the non-elected claim 20. Accordingly, claims 39-41 are not been further treated on the merits.

***35 U.S.C. 103(a) rejection***

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

**Claims 21-38 and 45** are rejected under 35 U.S.C. 103(a) as being unpatentable over Heath (U.S. Patent 5,973,137) in combination with Wiggins (U.S. Patent 5,637,687) in view of Kuroita et al. (U.S. Patent 5,990,302).

Heath teaches methods for the isolation of purified RNA from biological sources, including the reagents used in the method (abstract). The method of Heath comprises cell lysis and nucleic acid isolation (col.3, lines 49-52). Therefore in order to isolate nucleic acid from a cell or biological sample the first step requires cell lysis. Heath discloses a list of biological material containing mixtures of nucleic acids such as

biological fluids, cells, animal waste products and blood (col.5, lines 1-10) used to purify the undegraded RNA. The environmental samples taken from air, water, sediment and soil are encompassed by the prior art's animal waste products. Heath discloses the isolation of a wide range of RNA such as ribosomal RNA, messenger RNA and viral RNA (col.5, lines 15-21). Heath discloses the reagents for red blood cell lysis comprising ammonium chloride, sodium bicarbonate and EDTA (col.8, lines 1-18). It is noted that said lysis reagent is free of strong chaotrope such as guanidium salts and urea. The pH of the cell suspension reagent is in the range of 7.5-8.0 (col.8, lines 40-41). Furthermore, the prior art discloses that the pH in the range of 5.5 –8.0 lowers the RNA degradation (col.2, lines 24-32). Heath discloses anionic detergents in the form of salts of sodium, potassium and lithium of dodecyl sulfate as well as N-lauroyl sarcosine (col.6, lines 7-13). The non-ionic detergent such as Triton X-100 is also disclosed (col.1, line 56). Heath also discloses the use of the alkali-metal salt such as sodium chloride and potassium chloride in the concentration of 2- 5.5 M (col.7, lines 1-9). Heath differs from the applicant's invention that Heath's method of purifying RNA does not provide the steps of using a solid support to isolate RNA from the lysate.

Wiggins teaches the compositions containing detergents and solid support matrix and methods for isolating nucleic acids from biological tissues and cells (abstract). Wiggins discloses the use of LiCl salt in a concentration of 2-5 M preferably 4 M (col. 12, lines 25-35 and Col. 18, Example 4). Wiggins also discloses that the use of LiCl solution helps to solubilize interfering nucleic acid contaminants (col. 14, lines 10-20).

Wiggins discloses the use of a solid support matrix in the purification of precipitated nucleic acid (col. 4, lines 60-65). Furthermore, Wiggins discloses the use of various detergents, surfactants and buffers (col. 10, lines 40-60).

The prior arts set forth supra are silent with regard to the alkali-metal salt concentration up to 10 M, however it would be within the scope of the artisan in this art to modify the alkali-metal salt concentration range between 4-10 M because Heath teaches the use of 2-5.5 m and Wiggins teaches that the alkali-metal salt such as LiCl helps to solubilize the contaminants in the nucleic acid purification.

Kuroita et al. teach the nucleic acid-binding solid support selected from the group consisting of silica and non-silica solid support such as silica, cellulose, nitrocellulose, latex and hydroxyapatite in col. 3, lines 3-5, that may have a form of particle, filter, reaction container and the like (col. 5, lines 20-22) in the isolation of RNA. Kuroita et al. disclosed the isolation of RNA from a sample of cells by mixing the sample with an RNA lysing solution containing a lithium salt and a chaotropic agent, forming a lysate, contacting lysate with a nucleic acid binding carrier such as silica particles, washing the solid support with an RNA wash solution (100 mM) and eluting the bound RNA from solid support. (col. 2, lines 44-60). Kuroita et al. also suggest in col. 3, lines 41-50, the RNA biological sample can be , for example, serum, blood, tissue, urine, saliva, virus and bacteria or fungus. Furthermore, in col. 6, lines 41-63, Kuroita et al. disclosed mixing a biological material containing RNA with the lysing solution and a silica solid support, washing the solid support with an RNA wash solution and then eluting the

bound undegraded RNA from the solid support. Therefore, it would be within the scope of the artisan in this art to replace silica with a non-silica solid support through routine experimentation in the absence of unexpected results with a particular solid support. With regard to the solid support contained in a vessel such as cartridge or centrifuge tubes, it would be within the scope of the artisan in this art to use these vessels to hold the solid support in the course of routine purification experimentation.

Therefore, it would have been obvious to person having ordinary skill in the art at the time the invention was made, to modify the method of Heath, which teaches cell lysis to release RNA in combination with Wiggins, which teaches the use of alkali-metal salt such as LiCl which helps to solubilize interfering nucleic acid contaminants and the purification of an undegraded RNA from a lysate sample using a solid support of Kuroita et al. The ordinary artisan would also have been motivated to have produced a solid support which was pre-treated with a lysing solution for the expected benefit of low cost and disposability. Those skilled in the art would be motivated to obtain the RNA sample in high purity from a biological source because the cells or viral protein coats can be lysed to release undegraded RNA because the Rnases responsible for RNA degradation are inactivated during lysis (Heath: col.1, lines 18-22) and the use of a solid support in the purification of RNA greatly increase the yield and purity of the isolated RNA (Kuroita et al.: col.2, lines 48-50).

Any inquiry concerning this communication or earlier communications from the

Examiner should be directed to Devesh Khare whose telephone number is (571)272-0653. The examiner can normally be reached on Monday to Friday from 8:00 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anna Jiang, Supervisory Patent Examiner, Art Unit 1623 can be reached at (571)272-0627. The official fax phone numbers for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Devesh Khare, Ph.D.,J.D.
Art Unit 1623

August 11, 2006